m-Nitrobenzoic Acid

CAS #121-9
Swiss CD-1 mice, at 0.0, .35, 0.75, and 1.50% in feed
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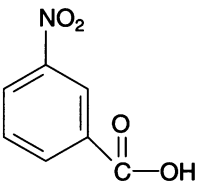

m-Nitrobenzoic acid (MNB) is widely used in explosive and dyestuff industries and also as a chemical intermediate in organic syntheses. In a 90-day prechronic study, both F344 rats and B6C3F1 mice exposed to high concentrations of MNB exhibited testicular atrophy and reduced sperm count. This RACB study using Swiss CD-1 mice was performed as a follow-up to that original observation. Data from a 2-week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation study at 0.35, 0.75, and 1.5% in feed. Based on mean feed consumption and body weight, the estimated daily dosages were approximately 0.5, 1.3, and 2.8 g/kg/day.

During Task 2, four, three, two, and three animals died from causes ranging from lymphoma to ruptures to partner-inflicted wounds to a variety of infections. There was no clear relationship to MNB exposure. During Task 2, postpartum dam weights in the middle and high dose groups were approximately 5 to 8% and approximately 12 to 14% lower than controls, respectively. Male body weights were reduced only at the high dose by approximately 9%. Daily feed consumption was increased by approximately 10% at the high dose.

Reproductive performance was impaired during Task 2. Mice in the middle and high dose groups delivered approximately 10 and 27% fewer pups per litter, respectively. At the high dose, there were 14% fewer litters per pair and a 14% reduction in adjusted pup weight. In addition, the high dose group took from 5 to 7 days longer to deliver the third, fourth and fifth litters, a significant increase.

The last litter was reared by the dam until weaning. Preweaning pup mortality was increased at the high dose: about half the pups died before weaning, and the remaining pups weighed 30 to 40% less than their respective controls. The only effect at the middle dose was a 15% reduction in male pup weight at postnatal day 21.

After the last litter was reared, a crossover test (Task 3) was conducted with the control and high dose mice. There was a 33% reduction in the number of mated females who delivered a litter in the group containing treated females. Pup indices were reduced only in litters from treated females: they delivered 50% fewer pups per litter, and those pups weighed approximately 10% less than their controls.

After the crossover pups were delivered and evaluated, the control and high dose F_0 adults were killed and necropsied. Treated female body weight was reduced by 13%, and adjusted kidney weight was approximately 7% lower in the 1.5% MNB females than in their controls. While there was no change in estrous cycle parameters or length, there were more cystic ovaries in the treated group (3/11) than in the controls (1/22). Male body weight at the high dose was reduced by approximately 10% and adjusted liver weight was increased by approximately 6%. Sperm indices were unchanged.

The F_1 mice from all dose groups were reared on the same diet that was provided their parents and cohabited within dose groups at approximately postnatal day 74. At the high dose, there was an approximately 20% reduction in live pup number, while adjusted pup weight was reduced in the middle and high dose groups by 13 and 21%, respectively.

After the F_2 litters were delivered and evaluated, the F_1 adults were killed and necropsied. Female body weight was reduced in the middle and high dose groups by 5 and 23%, respectively. Adjusted liver weight was increased by approximately 12% at the high dose; estrous cycle parameters were unchanged across dose groups. Male body weight was reduced by 10 and 18% in the middle and high dose groups, respectively. Adjusted kidney weight was reduced by approximately 10% at the high dose only. No significant treatment-related microscopic lesions were noted in the reproductive organs of these animals.

Thus, m-nitrobenzoic acid reduced weight gain in adults and caused significant reproductive toxicity in both generations. The second generation was not clearly more affected than the first. The female appeared more sensitive than the male, and though body weight was reduced, nonreproductive toxicities (organ weight changes, microscopic lesions) were not marked.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB90256058**
Chemical: **m-Nitrobenzoic acid**
CAS#: **121-92-6**
Mode of exposure: **Feed**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.35%	0.75%	1.50%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, ↓	↓, ↓
Kidney weight[a]	•	•	—, ↓
Liver weight[a]	•	•	↑, —
Mortality	—, —	—, —	—, —
Feed consumption	—, —	—, —	—, ↑
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	↓
# live pups/litter; pup wt./litter	—, —	↓, —	↓, ↓
Cumulative days to litter	—	—	↑
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	—

Determination of affected sex (crossover)	Male	Female	Both
Dose level	—	1.5%	—

F_1 generation — Dose concentration →	0.35%	0.75%	1.50%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	—, —	↓, —	↓, ↓
Mortality	—, —	—, —	↑, ↑
Adult body weight	—, —	↓, ↓	↓, ↓
Kidney weight[a]	—, —	—, —	↓, —
Liver weight[a]	—, —	—, —	—, ↑
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
Fertility index	—	—	—
# live pups/litter; pup wt./litter	—, —	—, ↓	↓, ↓
Absolute testis, epididymis weight[a]	—, —	—, —	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	—, —	—, —	—, —
Epidid. sperm parameters (#, motility, morphology)	—, —, —	—, —, —	—, —, —
Estrous cycle length	—	—	—

Summary information	
Affected sex?	**Female**
Study confounders:	**None**
NOAEL reproductive toxicity:	**0.35%**
NOAEL general toxicity:	**0.35%**
F_1 more sensitive than F_0?	**No**
Postnatal toxicity:	**Yes**

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.